MSH2 gene

mutS homolog 2

Normal Function

The *MSH2* gene provides instructions for making a protein that plays an essential role in DNA repair. This protein helps fix mistakes that are made when DNA is copied (DNA replication) in preparation for cell division. The MSH2 protein joins with one of two other proteins, MSH6 or MSH3 (each produced from a different gene), to form a protein complex. This complex identifies locations on the DNA where mistakes have been made during DNA replication. Another group of proteins, the MLH1-PMS2 protein complex, then repairs the errors. The *MSH2* gene is a member of a set of genes known as the mismatch repair (MMR) genes.

Health Conditions Related to Genetic Changes

Lynch syndrome

About 40 percent of all cases of Lynch syndrome with an identified gene mutation are associated with inherited mutations in the *MSH2* gene. Lynch syndrome increases the risk of many types of cancer, particularly cancers of the colon (large intestine) and rectum, which are collectively referred to as colorectal cancer. People with Lynch syndrome also have an increased risk of cancers of the endometrium (lining of the uterus), ovaries, stomach, small intestine, liver, gallbladder duct, upper urinary tract, and brain.

MSH2 gene mutations involved in Lynch syndrome may cause the production of an abnormally short or inactive MSH2 protein that cannot perform its normal function. When the MSH2 protein is absent or nonfunctional, the number of DNA mistakes that are left unrepaired during cell division increases substantially. The errors accumulate as the cells continue to divide, which may cause the cells to function abnormally, increasing the risk of tumor formation in the colon or another part of the body.

Some mutations in the *MSH2* gene cause a variant of Lynch syndrome called Muir-Torre syndrome. In addition to colorectal cancer, people with this condition have an increased risk of developing several uncommon skin tumors. These rare skin tumors include sebaceous adenomas and carcinomas, which occur in glands that produce an oily substance called sebum (sebaceous glands). Multiple rapidly growing tumors called keratoacanthomas may also occur, usually on sun-exposed areas of skin.

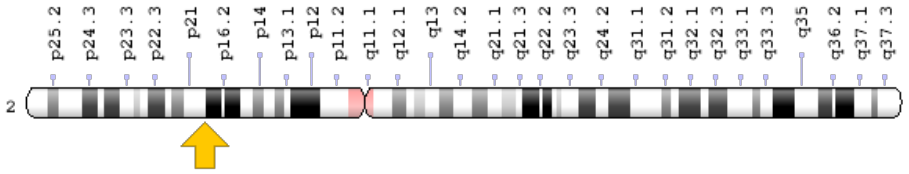
ovarian cancer

Inherited changes in the *MSH2* gene increase the risk of developing ovarian cancer, as well as other types of cancer, as part of Lynch syndrome (described above). Women with Lynch syndrome have an 8 to 10 percent chance of developing ovarian cancer in their lifetimes, as compared with 1.6 percent in the general population.

Chromosomal Location

Cytogenetic Location: 2p21-p16.3, which is the short (p) arm of chromosome 2 between positions 21 and 16.3

Molecular Location: base pairs 47,403,067 to 47,634,501 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- COCA1
- HNPCC
- HNPCC1
- MSH2_HUMAN
- mutS (E. coli) homolog 2
- mutS (E. coli) homolog 2 (colon cancer, nonpolyposis type 1)
- mutS homolog 2, colon cancer, nonpolyposis type 1 (E. coli)

Additional Information & Resources

Educational Resources

- American Medical Association and National Coalition for Health Professional Education in Genetics: Understand the Basics of Genetic Testing for Hereditary Colorectal Cancer
  http://www.nchpeg.org/documents/crc/Basics%20of%20genetic%20testing.pdf
- Cancer Medicine (sixth edition, 2003): DNA Mismatch Repair Gene Defects and HNPCC
  https://www.ncbi.nlm.nih.gov/books/NBK12469/#A1595
- Molecular Biology of the Cell (fourth edition, 2002): Defects in DNA Mismatch Repair Provide an Alternative Route to Colorectal Cancer
  https://www.ncbi.nlm.nih.gov/books/NBK26902/#A4345

GeneReviews

- Lynch Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1211

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28MSH2%5BTI%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- MUIR-TORRE SYNDROME
  http://omim.org/entry/158320
- MutS, E. COLI, HOMOLOG OF, 2
  http://omim.org/entry/609309

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/MSH2ID340ch2p22.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MSH2%5Bgene%5D
- HGNC Gene Family: MutS homologs
  http://www.genenames.org/cgi-bin/genefamilies/set/1026

- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=7325
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4436
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